Cold Weather Seasonality of Gastroenteritis Associated with Norwalk-like Viruses

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Norwalk-like viruses (NLVs) are the most common cause of acute nonbacterial gastroenteritis in adults, but little is known about their seasonality. The lack of specific diagnostic tools impeded study of these viruses in the past, and surveys using electron microscopy often grouped NLVs with other unrelated viruses. A search of the scientific literature found eight surveys of gastroenteritis, which were conducted for at least 1 year, that specifically identified NLVs. Unpublished data from laboratories of 4 NLV researchers were also used. These surveys, which were conducted in eight countries, reported sporadic cases and outbreaks of NLV-associated gastroenteritis among all age groups. The monthly occurrence of these cases and outbreaks was plotted, and while transmission occurred year-round in most surveys, a cold weather peak was demonstrated in 11 of the 12 studies. This key epidemiologic feature of the viruses has important implications concerning their mode of transmission and for understanding the etiology of acute gastroenteritis in adults.

Since the initial description of the Norwalk virus in 1972, Norwalk-like viruses (NLVs; also called small round structured viruses [SRSV]) have come to be recognized as the most common cause of outbreaks of acute, nonbacterial gastroenteritis [1]. NLVs are spread by the fecal-oral route, and outbreaks are often traced to contaminated food or water. However, transmission by airborne droplets or person-to-person contact have also been suggested to explain the many outbreaks in which another mode of spread cannot be identified [2].

The inability to culture NLVs and the lack of a simple, sensitive assay to detect them in clinical and environmental specimens have hampered epidemiologic studies. Early studies employed electron microscopy for detection, but NLVs were often grouped with the “classic caliciviruses” (which are now called Sapporo-like viruses), astroviruses, and small round viruses (e.g., enteroviruses)—organisms that may have different epidemiologic features and transmission characteristics. Newly developed molecular assays, including reverse transcriptase–polymerase chain reaction (RT-PCR) and antigen-specific ELISAs, have facilitated the study of NLVs, resulting in a wealth of new information regarding the epidemiology of these viruses.

In reviewing our own epidemiologic data on recently investigated outbreaks of gastroenteritis [3], we observed winter peaks in NLV-associated outbreaks over the last 3 years. A winter seasonal peak in NLV-associated gastroenteritis has been noted by others also [4, 5], but a winter peak has not been universally reported, and textbooks still describe a summer pattern [6, 7]. To resolve this apparent discrepancy, we reviewed 12 studies of gastroenteritis, including some in which new diagnostics have been used, in order to describe the seasonality of disease caused by NLVs and to gain insights into what this seasonal pattern might mean for disease transmission.

Methods

For this review, we examined the results of surveys of NLV outbreaks and sporadic cases identified from a MEDLINE search of articles published from 1975 to 1998, using the key words SRSV, Norwalk, and gastroenteritis. We also identified reference laboratories that have compiled similar data on the seasonal distribution of NLVs in three different countries: Gifu Prefectural Institute of Health and Environmental Science, Gifu, Japan; Statens Serum Institut, Copenhagen, Denmark; and the Research Laboratory for Infectious Diseases (RIVM), Bilthoven, The Netherlands.

We also reviewed surveillance reports from the National Institute of Infectious Diseases of Japan for the years 1995 and 1997–1998 (1996 data are unavailable); these data are reported on a monthly basis in the Infectious Agents Surveillance Report. In addition, we report our own outbreak surveillance data from the Centers for Disease Control and Prevention (CDC).

Studies were selected for analysis if they were conducted continuously for ≥1 year, reported outbreaks or sporadic cases of gastroenteritis on a monthly or weekly basis, and classified NLVs in a category distinct from small round viruses, astroviruses, or other classic caliciviruses.
We determined the seasonality of NLV-associated disease by plotting the percentage of the total number of annual cases or outbreaks that occurred in each month. The median number or percentage of the total number of annual NLV cases was determined for each study so that data for 6 months of the study were above the median and data for the other 6 months were below this value. A seasonal peak was defined as a period of 3 consecutive months when the monthly proportion of NLV reports was above the median. Data from studies of outbreaks were examined separately from data collected from cases of sporadic disease.

Results

Twelve NLV surveys conducted during a 21-year period (1978 through 1998) in eight countries were included in our analysis (table 1). Two studies included only children [8, 9], and the remainder included patients of all ages [10–17]. All investigators used electron microscopy as a reference method, and six of the eight surveys used RT-PCR for virus detection after 1993.

NLVs were reported throughout the year, except in one study from Australia [12], where no NLVs were detected in the summer months (figure 1). A remarkable finding in all studies and in all countries was that the low point for disease reports for both sporadic cases and outbreaks occurred in the warm months of summer. NLV-associated gastroenteritis reports peaked in the winter in 10 of 12 surveys. In one survey from Yorkshire, England [9], and in one from southeastern Australia [17], NLVs were reported predominantly in cold weather months but peaked in spring or early summer. This seasonality was present even where outbreaks occurred in institutions or were traced to contaminated food. Seasonal variation was greatest in Japan, Canada, and The Netherlands and least in the United Kingdom and the United States. Seasonality did not appear to be related to the detection method used, age group, or suspected mode of transmission.

Discussion

The data from our study demonstrate the cold weather predominance of NLV-associated disease. The month in which illness peaked varied, but all surveys consistently reported a nadir in the warm summer months. This finding was independent of the study setting (i.e., outbreaks vs. sporadic cases), the age of the patients, or the detection methods used and has many implications concerning the route of transmission of NLVs.

Winter seasonal transmission is a key epidemiologic feature of rotavirus, another gastrointestinal pathogen for which airborne transmission has been postulated [18]. Other viruses with winter seasonality, such as respiratory syncytial virus, influenza, and measles, are known to be spread by respiratory droplets. The rapidity with which the NLVs can spread through a community has led some investigators to postulate that airborne spread also may be important for these viruses [2]. While NLVs are transmitted primarily by the fecal-oral route [1], the winter seasonality of NLV-associated disease would lend support to airborne spread as a secondary route. Of note, hospitalizations of adults for gastroenteritis are more common in winter months than in summer months.

Table 1. Summary of results of 12 surveys of Norwalk-like viruses (NLVs) in sporadic cases and outbreaks of gastroenteritis.

<table>
<thead>
<tr>
<th>Disease setting, location</th>
<th>Reference</th>
<th>Time period</th>
<th>Age group</th>
<th>No. a</th>
<th>Detection method(s)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>1/1996–12/1998</td>
<td>All</td>
<td>434</td>
<td></td>
<td>Regional PH laboratory</td>
<td></td>
</tr>
<tr>
<td>England and Wales</td>
<td>1/1990–12/1995</td>
<td>All</td>
<td>128</td>
<td>EM</td>
<td>Multiple laboratories</td>
<td></td>
</tr>
<tr>
<td>Outbreaks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Netherlands</td>
<td>c</td>
<td>1/1990–10/1998</td>
<td>All</td>
<td>139</td>
<td>EM, RT-PCR</td>
<td>Predominantly institutions, PH research laboratory</td>
</tr>
<tr>
<td>Japan (Tokyo)</td>
<td>[16] 12/1984–12/1987</td>
<td>All</td>
<td>80</td>
<td>IEM</td>
<td>53/80 were oyster associated</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>e</td>
<td>1/1994–12/1997</td>
<td>All</td>
<td>186</td>
<td>IEM, RT-PCR</td>
<td>CDC data</td>
</tr>
<tr>
<td>Australia (Victoria)</td>
<td>[17] 1/1980–1995</td>
<td>All</td>
<td>119</td>
<td>EM, RT-PCR</td>
<td>Outbreaks and sporadic cases</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: EM = electron microscopy; RT-PCR = reverse transcriptase–polymerase chain reaction; PH = public health; IEM = immune EM; CDC = Centers for Disease Control and Prevention.

a No. of patients with or outbreaks of NLV-associated gastroenteritis.

b Böttiger B (Statens Serum Institut, Copenhagen), personal communication.
c Koopmans M, unpublished data.
d Kawamoto H (Gifu Prefectural Institute of Bioindustrial Technology, Gifu, Japan), personal communication.
e Noel J, unpublished data.
Figure 1. Seasonal distribution of sporadic cases of gastroenteritis caused by Norwalk-like viruses. Horizontal dotted line on each graph represents median no. of cases per year; shaded areas indicate periods when no. of cases for at least 3 consecutive months are above median. For Japan (1994–1995, 97–98) and Australia (Victoria), nos. include both sporadic and outbreak cases.
even though the etiology of this illness is undetermined in >75% of hospitalized patients [19]. The winter seasonality of NLVs as a cause of gastroenteritis in adults suggests that the winter peak of undiagnosed gastroenteritis in hospitalized adults may be due in part to infections with NLVs.

The same winter peaks occurred for outbreaks of NLVs traced to foods. In Japan, many of the outbreaks and presumably some of the sporadic cases are related to the consumption of contaminated oysters but still display a marked seasonal distribution. This could be explained in part by regulations and cultural practices that encourage oyster consumption in winter months or by the filtering of sewage by oysters during seasonal NLV infections. Large regional outbreaks may also alter the observed seasonal pattern of reported disease when several years' data are combined; indeed, the peak incidence of disease does not consistently occur in the same month every year, even in the same region.

Long before the advent of modern diagnostic methods, clinicians recognized the syndrome “winter vomiting disease” [20]. However, later studies, including one from CDC [1], reported NLV-related outbreaks to be more common in the summer months. The CDC study found a slight predominance of summer-time outbreaks, but the finding was based on a relatively small number of observations over a 13-year period and used serology as the diagnostic tool. It excluded several outbreaks in which stool specimens were found with viruses that would likely have been classified as Norwalk-like in later studies using electron microscopy as a diagnostic tool.

The finding of a winter seasonality of NLVs provides important clues to the etiology of undiagnosed adult gastroenteritis hospitalizations and the mode of transmission of these viruses. The increasing availability of specific tools to study NLVs should shed more light on these important epidemiologic features in the future.

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References